

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

Page 12, second full paragraph:

Instead of the aforementioned recombinant human CRTH2-related protein, human tissue, a human cell strain, etc. in which natural human CRTH2 is highly expressed may be used in the present identification method. Alternatively, a transformant which has been transformed by a gene encoding the aforementioned human CRTH2-related protein may be used. In such a human tissue, human cell strain, etc., preferably, only human CRTH₂ is expressed, and the DP receptor and other prostanoid receptors are not expressed.

Page 15, first full paragraph:

When a selective modulator with respect to activation of human CRTH2, etc. is identified by means of the present identification method, no absolute limits are imposed on a test substance. Briefly, in the present identification method, a test substance may be a naturally occurring product (including a recombinant protein produced through biotechnological technique) or a chemically synthesized product. When the present identification method is carried out, if necessary, a known labeled or unlabeled ligand (for example, prostanoid such as ~~human~~-PGD₂) may be used.

Page 18, first full paragraph:

As described above, the properties of a test substance with respect to ~~human~~-prostaglandin D or a human prostaglandin D receptor are identified by correlating the effect of the substance on human CRTH2 (for example, a selective modulator effect) with the effect of the substance on the human prostaglandin D receptor. When the identification method is used for, for example, screening of drugs, it can greatly contribute to the relevant industry.

The paragraph bridging pages 20 and 21:

Each of KB8 cells, KD36 cells, and K562/neo cells was resuspended in Hank's balanced salt solution (HBSS, product of Gibco BRL) so as to attain a concentration of 3×10^7 cells/ml. The resultant suspension (0.1 ml) was placed in a 0.5-ml microtube, and then cooled on ice. Subsequently, 1 nM of [³H] PGD₂ (product of Amersham) which had been diluted with HBSS was added to the suspension, to thereby allow reaction to proceed on ice for one hour. The reacted cells were placed carefully onto

RPMI1640 medium (1 ml) containing 1 M sucrose and 10% fetal bovine serum, the medium having been placed in an 1.5-ml microtube and cooled by ice, and subjected to centrifugation (10,000 revolutions, three minutes) by use of a micro-centrifuge. After the supernatant was aspirated from the tube such that the mixture (about 0.1 ml) remained in the tube, the mixture was further subjected to centrifugation (10,000 revolutions, one minute) such that the reaction mixture did not remain on the tube wall, and subsequently the supernatant was removed as carefully as possible so as to avoid removing the cells. The radiation activity of the cells bound to [³H] PGD₂ was measured by use of a liquid scintillation counter. The radiation activity of the cells when measured, in a manner similar to that described above, in the presence of unlabeled PGD₂ (concentration: 200 times or more that of [³H] PGD₂) was used as an index of non-specific binding. As a result, as shown in Fig. 1, the specific binding of [³H] PGD₂ to K562/neo is not observed. In contrast, the specific binding of [³H] PGD₂ to KB8 or KD36 is observed. In this measurement system, anti CRTH2 antibody BM7 (Nagata, K. et al., J. Immunol., 162: 1278-1286, 1999 and Nagata, K., et al., FEBS Lett., 459: 195-199, 1999) selectively inhibited the binding of [³H] PGD₂ to KB8 in a concentration-dependent manner. The results show that this method can identify a selective modulator with respect to human CRTH2, which does not act on the DP receptor.

Page 23, third full paragraph:

[Example 6] Down modulation of human CRTH2 molecules by selective agonist.

IN THE CLAIMS:

The claims are amended as follows:

3. (amended) The identification method according to claim 1-~~or~~2, wherein binding ability, to human CRTH2 or a derivative thereof, of the test substance is used as an index of the property of the substance with respect to the human prostaglandin D receptor.

4. (amended) The identification method according to claim 1-~~or~~2, wherein in situ agonistic/antagonistic ability, to human CRTH2, of the test substance is used as an index of the property of the substance with respect to the human prostaglandin D receptor.